| L Number | Hits | Search Text | DB | Time stamp |
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| 1 | 23 | hadlaczky\$.in. | USPAT; | 2003/09/17 10:10 |
| | | | US-PGPUB; | |
| | | | EPO; JPO; | |
| | | | DERWENT | • |

L25 ANSWER 1 OF 19 MEDLINE

ACCESSION NUMBER: 2002008965 MEDLINE

DOCUMENT NUMBER: 21237598 PubMed ID: 11338924

TITLE: Satellite DNA-based artificial chromosomes for use in gene

therapy.

AUTHOR: Hadlaczky G

CORPORATE SOURCE: Institute of Genetics, Biological Research Center,

Hungarian Academy of Sciences, H-6701 Szeged, PO Box 521,

Hungary.. hgy@nucleus.szbk.u-szeged.hu

SOURCE: Curr Opin Mol Ther, (2001 Apr) 3 (2) 125-32. Ref: 33

Journal code: 100891485. ISSN: 1464-8431.

PUB. COUNTRY: England: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200112

ENTRY DATE: Entered STN: 20020121

Last Updated on STN: 20020121 Entered Medline: 20011205

AB Satellite DNA-based artificial chromosomes (SATACs) can be made by induced de novo chromosome formation in cells of different mammalian species. These artificially generated accessory chromosomes are composed of predictable DNA sequences and they contain defined genetic information. Prototype human SATACs have been successfully constructed in different cell types from 'neutral' endogenous DNA sequences from the short arm of the human chromosome 15. SATACs have already passed a number of hurdles crucial to their further development as gene therapy vectors, including: large-scale purification; transfer of purified artificial chromosomes into different cells and embryos; generation of transgenic animals and germline transmission with purified SATACs; and the tissue-specific expression of a therapeutic gene from an artificial chromosome in the milk of transgenic animals.

L25 ANSWER 2 OF 19 MEDLINE

ACCESSION NUMBER: 2000493348 MEDLINE

DOCUMENT NUMBER: 20297740 PubMed ID: 10841045

TITLE: Generation of transgenic mice and germline transmission of

a mammalian artificial chromosome introduced into embryos

by pronuclear microinjection.

AUTHOR: Co D O; Borowski A H; Leung J D; van der Kaa J; Hengst S;

Platenburg G J; Pieper F R; Perez C F; Jirik F R; Drayer J

Ι

CORPORATE SOURCE: Chromos Molecular Systems, Inc., Burnaby, British Columbia,

Canada.. dco@chromos.com

SOURCE: CHROMOSOME RESEARCH, (2000) 8 (3) 183-91.

Journal code: 9313452. ISSN: 0967-3849.

PUB. COUNTRY: Netherlands

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200010

ENTRY DATE: Entered STN: 20001027

Last Updated on STN: 20001027 Entered Medline: 20001016

We have generated transgenic mice by pronuclear microinjection of a murine satellite DNA-based artificial chromosome (SATAC). As 50% of the founder progeny were SATAC-positive, this demonstrates that SATAC transmission through the germline had occurred. FISH analyses of metaphase chromosomes from mitogen-activated peripheral blood lymphocytes from both the founder and progeny revealed that the

SATAC was maintained as a discrete chromosome and that it had not integrated into an endogenous chromosome. To our knowledge, this is the first report of the germline transmission of a genetically engineered mammalian artificial chromosome within transgenic animals generated through pronuclear microinjection. We have also shown that murine SATACs can be similarly introduced into bovine embryos. The use of embryo microinjection to generate transgenic mammals carrying genetically engineered chromosomes provides a novel method by which the unique advantages of chromosome-based gene delivery systems can be exploited.

L25 ANSWER 3 OF 19 MEDLINE

ACCESSION NUMBER: 2000019596 MEDLINE

DOCUMENT NUMBER: 20019596 PubMed ID: 10554168

TITLE:

Mammalian artificial chromosome pilot production facility: large-scale isolation of functional satellite DNA-based

artificial chromosomes.

deJong G; Telenius A H; Telenius H; Perez C F; Drayer J I; **AUTHOR:**

Hadlaczky G

Chromos Molecular Systems, Inc., Vancouver, British CORPORATE SOURCE:

Columbia, Canada.. gdejong@chromos.com

CYTOMETRY, (1999 Feb 1) 35 (2) 129-33. SOURCE:

Journal code: 8102328. ISSN: 0196-4763.

United States PUB. COUNTRY:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199911

ENTRY DATE: Entered STN: 20000113

> Last Updated on STN: 20000113 Entered Medline: 19991130

BACKGROUND: A pilot production facility has been established to isolate ABmammillian artificial chromosomes at high purity by using flow cytometric techniques. Dicentric chromosomes have been generated by the targeted amplification of pericentric heterochromatic and centromeric DNA by activating the "megareplicator." Breakage of these dicentric chromosomes generates satellite DNA-based artificial chromosomes (SATAC) from 60 to 400 megabases. METHODS: For large-scale production, we have developed cell lines capable of carrying one or two SATACs. A SATAC, because of a high adenine-thymine (AT) composition, is easily identified and sorted by using chromomycin A3 and Hoechst 33258 stains and a dual laser high-speed flow cytometer. A prototype SATAC (60 megabases) has been characterized. The prototype SATAC has been isolated from an original rodent/human hybrid cell line and transferred by using modified microcell fusion into a CHO production cell line. RESULTS: Metaphase chromosomes from this production cell line were isolated in a modified polyamine buffer, stained, and sorted by using a modified sheath buffer that maintains condensed chromosomes. SATACs are routinely sorted at rates greater than 1 million per hour. Sorted SATACs have been transferred to a variety of cells by using microcell fusion technology and were found to be functional. CONCLUSIONS: By developing new SATAC containing cell lines with fewer numbers of chromosomes in conjunction with operating a high speed flow sorter we have effectively generated an efficient production facility geared purely for the isolation of SATACS.

L25 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:336165 CAPLUS

DOCUMENT NUMBER: 136:96714

Satellite DNA-based artificial chromosomes for use in TITLE:

gene therapy

AUTHOR(S): Hadlaczky, Gyula

Institute of Genetics Biological Research Center, CORPORATE SOURCE:

Hungarian Academy of Sciences, Szeged, H-6701, Hung. Current Opinion in Molecular Therapeutics (2001), SOURCE:

3(2), 125-132

CODEN: CUOTFO; ISSN: 1464-8431

PharmaPress Ltd. PUBLISHER:

Journal; General Review DOCUMENT TYPE:

English LANGUAGE:

A review with refs. Satellite DNA-based artificial chromosomes (ABSATACs) can be made by induced de novo chromosome formation in cells of different mammalian species. These artificially generated accessory chromosomes are composed of predictable DNA sequences and they contain defined genetic information. Prototype human SATACs have been successfully constructed in different cell types from "neutral" endogenous DNA sequences from the short arm of the human chromosome 15. SATACs have already passed a no. of hurdles crucial to their further development as gene therapy vectors, including: large-scale purifn.; transfer of purified artificial chromosomes into different cells and embryos; generation of transgenic animals and germline transmission with purified SATACs; and the tissue-specific expression of a therapeutic gene from an artificial chromosome in the milk of transgenic

animals. THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 33 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2002 ACS L25 ANSWER 5 OF 19 ACCESSION NUMBER: 2000:716318 CAPLUS

DOCUMENT NUMBER:

134:232422

TITLE:

Satellite DNA-based artificial chromosomes-chromosomal

vectors. Reply to Comments

AUTHOR(S):

Brown, William R. A.

CORPORATE SOURCE:

Institute of Genetics, University of Nottingham,

Nottingham, UK

SOURCE:

Trends in Biotechnology (2000), 18(10), 403

CODEN: TRBIDM; ISSN: 0167-7799

PUBLISHER:

Elsevier Science Ltd.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

A polemic in response to Carl Perez et al. (ibid. 402-403). $\mathbf{A}\mathbf{B}$

L25 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2002 ACS 2000:716317 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

134:232421

TITLE:

Satellite DNA-based artificial chromosomes-chromosomal

vectors. Comments

AUTHOR (S):

Perez, Carl; de Jong, Gary; Drayer, Jan

CORPORATE SOURCE:

Chromos Molecular Systems Inc., Burnaby, BC, Can. Trends in Biotechnology (2000), 18(10), 402-403

CODEN: TRBIDM; ISSN: 0167-7799

PUBLISHER:

SOURCE:

Elsevier Science Ltd.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

A polemic in response to W.R.A. Brown et al. (ibid., 18(5), 218-223). ABAttention was brought to the existence of another chromosome-based vector technol. -- satellite DNA-based artificial chromosomes (SATACs).

REFERENCE COUNT:

THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS 16 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2002 ACS 2000:416625 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

133:39084

TITLE:

Artificial chromosomes, uses thereof and methods for

preparing artificialchromosomes

INVENTOR(S):

Hadlaczky, Gyula; Szalay, Aladar A.

PATENT ASSIGNEE(S):

Chromos Molecular Systems, Inc., Can.; The Biological Research Center of the Hungarian Academy of Sciences

SOURCE:

U.S., 55 pp., Cont.-in-part of U.S. Ser. No. 629,822,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
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                                             APPLICATION NO.
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             LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ,
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           AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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PRIORITY APPLN. INFO.:
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                                                           A2 19960715
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                                                           A 19960807
                                         WO 1997-US5911
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                                                              19980904
                                         US 1998-152031
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Methods for prepg. cell lines that contain artificial chromosomes, methods AΒ for prepn. of artificial chromosomes, methods for purifn. of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes that, except for inserted heterologous DNA, are substantially composed of heterochromatin are provided. Methods for use of the artificial chromosomes, including for gene therapy, prodn. of gene products and prodn. of transgenic plants and animals are also provided. Methods for prepg. cell lines that contain mammalian artificial chromosomes (MACs), methods for prepn. of artificial chromosomes, methods for purifn. of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes (SATACs) that, except for inserted heterologous DNA, are substantially composed of heterochromatin are provided; also provided are minichromosomes based on amplification of euchromatin. Methods for use of the artificial chromosomes, including for gene therapy, prodn. of gene products and prodn. of transgenic plants and animals are also provided.

REFERENCE COUNT:

THERE ARE 297 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

297

DOCUMENT NUMBER: 133:276928

TITLE: Generation of transgenic mice and germline

introduced into embryos by pronuclear microinjection

AUTHOR(S): Co, Deborah O.; Borowski, Anita H.; Leung, Josephine

D.; Van der Kaa, Jos; Hengst, Sandra; Platenburg, Gerard J.; Pieper, Frank R.; Perez, Carl F.; Jirik,

Frank R.; Drayer, Jan I.

CORPORATE SOURCE: Chromos Molecular Systems, Inc., Burnaby, BC, V5A 1W9,

Can.

SOURCE: Chromosome Research (2000), 8(3), 183-191

CODEN: CRRSEE; ISSN: 0967-3849

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal LANGUAGE: English

We have generated transgenic mice by pronuclear microinjection of a murine \mathbf{AB} satellite DNA-based artificial chromosome (SATAC). As 50% of the founder progeny were SATAC-pos., this demonstrates that SATAC transmission through the germline had occurred. FISH analyses of metaphase chromosomes from mitogen-activated peripheral blood lymphocytes from both the founder and progeny revealed that the SATAC was maintained as a discrete chromosome and that it had not integrated into an endogenous chromosome. To our knowledge, this is the first report of the germline transmission of a genetically engineered mammalian artificial chromosome within transgenic animals generated through pronuclear microinjection. We have also shown that murine SATACs can be similarly introduced into bovine embryos. of embryo microinjection to generate transgenic mammals carrying genetically engineered chromosomes provides a novel method by which the unique advantages of chromosome-based gene delivery systems can be exploited.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:114388 CAPLUS

DOCUMENT NUMBER: 132:147617

TITLE: Artificial chromosomes, uses thereof and methods for

preparing artificial chromosomes

INVENTOR(S): Hadlaczky, Gyula; Szalay, Aladar A.

PATENT ASSIGNEE(S): Chromos Molecular Systems, Inc., Can.; The Biological

Research Center of the Hungarian Academy of Sciences U.S., 59 pp., Cont.-in-part of U.S. Ser. No. 682,080.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

SOURCE:

| PATENT N | Ю. | | KI | ND : | DATE | | | A | PPLI | CATI | ON NO | ο. | DATE | | | |
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| US 60251 | .55 | | Α | | 2000 | 0215 | | U | S 19 | 96-6 | 9519 | 1 | 19960 | 0807 | | |
| US 60776 | 97 | | Α | , | 2000 | 0620 | | U | S 19 | 96-6 | 8208 | 0 | 19960 | 0715 | | |
| CA 22506 | 82 | | \mathbf{A} | A | 1997 | 1030 | | C | A 19 | 97-2 | 2506 | 82 | 19970 | 0410 | | |
| WO 97401 | 83 | | A: | 2 | 1997 | 1030 | | W | 0 19 | 97-U | S591 | 1 | 19970 | 0410 | | |
| WO 97401 | 83 | | A. | 3 | 19980 | 0205 | | | | | | | | | | |
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PRIORITY APPLN. INFO.:
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                                        US 1996-695191
                                        WO 1997-US5911 W 19970410
                                        US 1998-99214P P 19980904
                                                         B2 19980911
                                        US 1998-152031
    Methods for prepg. cell lines that contain mammalian artificial
AB
     chromosomes (MACs), methods for prepn. of artificial chromosomes, methods
     for purifn. of artificial chromosomes, methods for targeted insertion of
     heterologous DNA into artificial chromosomes, and methods for delivery of
     the chromosomes to selected cells and tissues are provided. Also provided
     are cell lines for use in the methods, and cell lines and chromosomes
    produced by the methods. In particular, satellite artificial chromosomes
     (SATACs) that, except for inserted heterologous DNA, are
     substantially composed of heterochromatin are provided; also provided are
    minichromosomes based on amplification of euchromatin. Methods for use of
     the artificial chromosomes, including for gene therapy, prodn. of gene
    products and prodn. of transgenic plants and animals are also provided.
                               THERE ARE 318 CITED REFERENCES AVAILABLE FOR
REFERENCE COUNT:
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                               THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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                      CAPLUS COPYRIGHT 2002 ACS
L25
    ANSWER 10 OF 19
                         1997:718036 CAPLUS
ACCESSION NUMBER:
                         128:19355
DOCUMENT NUMBER:
                         methods for prepq. mammalian artificial chromosomes
TITLE:
                         (MACs)
                         Hadlaczky, Gyula; Szalay, Aladar A.
INVENTOR(S):
                         Hadlaczky, Gyula, Hung.; Szalay, Aladar A.; American
PATENT ASSIGNEE(S):
                         Gene Therapy, Inc.; Biological Research Center of the
                         Hungarian Academy of Sciences; Loma Linda University
                         PCT Int. Appl., 248 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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                                           APPLICATION NO.
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                                           WO 1997-US5911
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             LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
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BR 9708855 20000104 Α BR 1997-8855 19970410 JP 2000508177 T2 JP 1997-538116 20000704 19970410 PRIORITY APPLN. INFO.: US 1996-629822 A 19960410 US 1996-682080 A 19960715 US 1996-695191 A 19960807 US 1996-682191 A 19960715 WO 1997-US5911 W 19970410

AB Methods for prepg. cell lines that contain artificial chromosomes, methods for prepn. of artificial chromosomes, methods for purifn. of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes [SATACS] that, except for inserted heterologous DNA, are substantially composed of heterochromatin, are provided. Methods for use of the artificial chromosomes, including for gene therapy, prodn. of gene products and prodn. of transgenic plants and animals are also provided.

L25 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1995:625670 CAPLUS

DOCUMENT NUMBER: 123:37587

TITLE: Beneficiation of iron and manganese ores and recycling

of metal bearing slags by means of air-pulsated BATAC

jigs

AUTHOR(S): Wasmuth, Hans-Dieter; Ziaja, Dieter

CORPORATE SOURCE: Department Mineral Dressing Plants, KHD Humboldt Wedag

AG, Cologne, Germany

SOURCE: Prog. Miner. Process. Technol., Proc. Int. Miner.

Process. Symp., 5th (1994), 49-56. Editor(s): Demirel, Halim; Ersayin, Salih. Balkema: Rotterdam,

Neth.

CODEN: 61LDAB

DOCUMENT TYPE: Conference LANGUAGE: English

AB After minor modifications in design, the air pulsated BATAC jig a well known std. equipment for the prepn. of coal - can also be used for upgrading of intergrown hematite iron ores and manganese ores - lump ores as well as sinter fines, which require high sepn. densities to obtain marketable conc. grades. Furthermore the 8ATAC jig is also an appropriate unit for the recovery of the metal compds. of metal bearing slags.

SATAC jigs are in com. operation in two big iron ore beneficiation plants in Australia and Brazil since many years. Furthermore, recently orders have been received for BATAC jigs to be used for beneficiation of manganese ores in Ghana and Namibia and recycling of ferrochromium slags in South Africa. The typical design of these BATAC jigs with their very sensitive stratification and discharge devices for efficient processing of ores and slags are described, and the particular flowsheets and design concepts of the new jigging plants are presented.

L25 ANSWER 12 OF 19 USPATFULL

ACCESSION NUMBER: 2001:110143 USPATFULL

TITLE: ARTIFICIAL CHROMOSOMES, USES THEREOF AND METHODS FOR

PREPARING ARTIFICIAL CHROMOSOMES

INVENTOR(S): HADLACZKY, GYULA, SZAMOS, Hungary

SZALAY, ALADAR A., HIGHLAND, CA, United States

NUMBER KIND DATE

PATENT INFORMATION: US 2001008025 A1 20010712
APPLICATION INFO.: US 1998-96648 A1 19980612 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1996-629822, filed on 10

Apr 1996, ABANDONED

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: STEPHANIE L. SEIDMAN, HELLER EHRMAN WHITE & MCAULIFFE,

4250 EXECUTIVE SQUARE, 7TH FLOOR, LA JOLLA,, CA,

92037-9103

NUMBER OF CLAIMS: 63 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 5 Drawing Page(s)

LINE COUNT: 3855

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Methods for preparing cell lines that contain artificial chromosomes, methods for preparation of artificial chromosomes, methods for purification of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes that, except for inserted heterologous DNA, are substantially composed of heterochromatin are provided. Methods for use of the artificial chromosomes, including for gene therapy, production of gene products and production of transgenic plants and animals are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 13 OF 19 USPATFULL

ACCESSION NUMBER: 2000:77213 USPATFULL

TITLE: Artificial chromosomes, uses thereof and methods for

preparing artificial chromosomes

INVENTOR(S): Hadlaczky, Gyula, Szamos, Hungary

Szalay, Aladar A., Highland, CA, United States

PATENT ASSIGNEE(S): Chromos Molecular Systems, Inc., Canada (non-U.S.

corporation)

The Biological Research Center of the Hungarian Academy

of Sciences, Hungary (non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 6077697 20000620 APPLICATION INFO.: US 1996-682080 19960715 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-629822, filed

on 10 Apr 1996, now abandoned

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Railey, II, Johnny F.

LEGAL REPRESENTATIVE: Seidman, Stephanie L.Heller, Ehrman, White & McAuliffe

NUMBER OF CLAIMS: 64 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)

LINE COUNT: 4703

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Methods for preparing cell lines that contain artificial chromosomes, methods for preparation of artificial chromosomes, methods for purification of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes that, except for inserted heterologous DNA, are substantially composed of heterochromatin are provided. Methods for use of the artificial chromosomes, including for gene therapy, production of gene products and production of transgenic plants and animals are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 14 OF 19 USPATFULL

PATENT ASSIGNEE(S):

ACCESSION NUMBER: 2000:18241 USPATFULL

Artificial chromosomes, uses thereof and methods for TITLE:

preparing artificial chromosomes

INVENTOR(S): Hadlaczky, Gyula, Szamos, Hungary

Szalay, Aladar A., Highland, CA, United States Chromos Molecular Systems, Inc., Canada (non-U.S.

corporation)

The Biological Research Center of the Hungarian Academy

of Sciences, Hungary (non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 6025155 20000215 APPLICATION INFO.: US 1996-695191 19960807 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-682080, filed

on 15 Jul 1996 which is a continuation-in-part of Ser. No. US 1996-629822, filed on 10 Apr 1996, now abandoned

Utility DOCUMENT TYPE: FILE SEGMENT: Granted

Railey, II, Johnny F. PRIMARY EXAMINER:

LEGAL REPRESENTATIVE: Seidman, Stephanie L. Heller Ehrman White & McAuliffe

NUMBER OF CLAIMS: 37 EXEMPLARY CLAIM:

5 Drawing Figure(s); 5 Drawing Page(s) NUMBER OF DRAWINGS:

LINE COUNT: 5465

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Methods for preparing cell lines that contain artificial chromosomes, ABmethods for preparation of artificial chromosomes, methods for purification of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes that, except for inserted heterologous DNA, are substantially composed of heterochromatin are provided. Methods for use of the artificial chromosomes, including for gene therapy, production of

gene products and production of transgenic plants and animals are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 15 OF 19 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001161268 EMBASE

Satellite DNA-based artificial chromosomes for use in gene TITLE:

therapy.

AUTHOR: Hadlaczky G.

CORPORATE SOURCE: G. Hadlaczky, Institute of Genetics, Biological Research

Center, Hungarian Academy of Sciences, PO Box 521, H-6701

Szeged, Hungary. hgy@nucleus.szbk.u-szeged.hu

Current Opinion in Molecular Therapeutics, (2001) 3/2 SOURCE:

(125-132). Refs: 33

ISSN: 1464-8431 CODEN: CUOTFO

COUNTRY: United Kingdom DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics

> 029 Clinical Biochemistry

LANGUAGE: English SUMMARY LANGUAGE: English

Satellite DNA-based artificial chromosomes (SATACs) can be made ABby induced de novo chromosome formation in cells of different mammalian species. These artificially generated accessory chromosomes are composed of predictable DNA sequences and they contain defined genetic information. Prototype human SATACs have been successfully constructed in different cell types from 'neutral' endogenous DNA sequences from the short arm of the human chromosome 15. SATACs have already passed a number of hurdles crucial to their further development as gene therapy vectors, including: large-scale purification; transfer of purified artificial chromosomes into different cells and embryos; generation of transgenic animals and germline transmission with purified SATACs; and the tissue-specific expression of a therapeutic gene from an artificial chromosome in the milk of transgenic animals.

L25 ANSWER 16 OF 19 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000171063 EMBASE

TITLE: Generation of transgenic mice and germline transmission of

a mammalian artificial chromosome introduced into embryos

by pronuclear microinjection.

AUTHOR: Co D.O.; Borowski A.H.; Leung J.D.; Van der Kaa J.; Hengst

S.; Platenburg G.J.; Pieper F.R.; Perez C.F.; Jirik F.R.;

Drayer J.I.

CORPORATE SOURCE: D.O. Co, Chromos Molecular Systems, Inc., 8081 Loughheed

Highway, Burnaby, BC V5A 1W9, Canada. dco@chromos.com

SOURCE: Chromosome Research, (2000) 8/3 (183-191).

Refs: 35

ISSN: 0967-3849 CODEN: CRRSEE

COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics

029 Clinical Biochemistry

LANGUAGE: English SUMMARY LANGUAGE: English

We have generated transgenic mice by pronuclear microinjection of a murine ABsatellite DNA-based artificial chromosome (SATAC). As 50% of the founder progeny were SATAC-positive, this demonstrates that SATAC transmission through the germline had occurred. FISH analyses of metaphase chromosomes from mitogen-activated peripheral blood lymphocytes from both the founder and progeny revealed that the SATAC was maintained as a discrete chromosome and that it had not integrated into an endogenous chromosome. To our knowledge, this is the first report of the germline transmission of a genetically engineered mammalian artificial chromosome within transgenic animals generated through pronuclear microinjection. We have also shown that murine SATACs can be similarly introduced into bovine embryos. The use of embryo microinjection to generate transgenic mammals carrying genetically engineered chromosomes provides a novel method by which the unique advantages of chromosome-based gene delivery systems can be exploited.

L25 ANSWER 17 OF 19 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999041146 EMBASE

TITLE: Mammalian artificial chromosome pilot production facility:

Large-scale isolation of functional satellite DNA-based

artificial chromosomes.

AUTHOR: deJong G.; Telenius A.H.; Telenius H.; Perez C.F.; Drayer

J.I.; Hadlaczky G.

CORPORATE SOURCE: G. deJong, Chromos Molecular Systems, Inc., 6660 Northwest

Marine Drive, Vancouver, BC V6T 1Z4, Canada.

gdejong@chromos.com

SOURCE: Cytometry, (1 Feb 1999) 35/2 (129-133).

Refs: 12

ISSN: 0196-4763 CODEN: CYTODQ

COUNTRY: United States
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 021 Developmental Biology and Teratology

022 Human Genetics

029 Clinical Biochemistry

LANGUAGE: English SUMMARY LANGUAGE: English

Background: A pilot production facility has been established to isolate mammalian artificial chromosomes at high purity by using flow cytometric techniques. Dicentric chromosomes have been generated by the targeted amplification of pericentric heterochromatic and centromeric DNA by activating the 'megareplicator.' Breakage of these dicentric chromosomes generates satellite DNA-based artificial chromosomes (SATAC) from 60 to 400 megabases. Methods: For large-scale production, we have developed cell lines capable of carrying one or two SATACS. A SATAC, because of a high adenine- thymine (AT) composition, is easily identified and sorted by using chromomycin A3 and Hoechst 33258 stains and a dual laser high-speed flow cytometer. A prototype SATAC (60 megabases) has been characterized. The prototype SATAC has been isolated from an original rodent/human hybrid cell line and transferred by using modified microcell fusion into a CHO production cell line. Results: Metaphase chromosomes from this production cell line were isolated in a modified polyamine buffer, stained, and sorted by using a modified sheath buffer that maintains condensed chromosomes. SATACs are routinely sorted at rates greater than 1 million per hour. Sorted SATACs have been transferred to a variety of cells by using microcell fusion technology and were found to be functional. Conclusions: By developing new SATAC containing cell lines with fewer numbers of chromosomes in conjunction with operating a high speed flow sorter we have effectively generated an efficient production facility geared purely for the isolation of SATACs.

L25 ANSWER 18 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:324274 BIOSIS DOCUMENT NUMBER: PREV200000324274

TITLE: Generation of transgenic mice and germline transmission of

a mammalian artificial chromosome introduced into embryos

by pronuclear microinjection.

AUTHOR(S): Co, Deborah O. (1); Borowski, Anita H.; Leung, Josephine D.

(1); van der Kaa, Jos; Hengst, Sandra; Platenburg, Gerard J.; Pieper, Frank R.; Perez, Carl F. (1); Jirik, Frank R.;

Drayer, Jan I. (1)

CORPORATE SOURCE: (1) Chromos Molecular Systems, Inc., 8081 Lougheed Highway,

Burnaby, British Columbia, V5A 1W9 Canada

SOURCE: Chromosome Research, (2000) Vol. 8, No. 3, pp. 183-191.

print.

ISSN: 0967-3849.

DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

We have generated transgenic mice by pronuclear microinjection of a murine satellite DNA-based artificial chromosome (SATAC). As 50% of the founder progeny were SATAC-positive, this demonstrates that SATAC transmission through the germline had occurred. FISH analyses of metaphase chromosomes from mitogen-activated peripheral blood lymphocytes from both the founder and progeny revealed that the SATAC was maintained as a discrete chromosome and that it had not integrated into an endogenous chromosome. To our knowledge, this is the first report of the germline transmission of a genetically engineered mammalian artificial chromosome within transgenic animals generated through pronuclear microinjection. We have also shown that murine SATACS can be similarly introduced into bovine embryos. The use of embryo microinjection to generate transgenic mammals carrying genetically engineered chromosomes provides a novel method by which the unique advantages of chromosome-based gene delivery systems can be exploited.

L25 ANSWER 19 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1999:104500 BIOSIS DOCUMENT NUMBER: PREV199900104500

TITLE: Mammalian artificial chromosome pilot production facility:

Large-scale isolation of functional satellite DNA-based

artificial chromosomes.

AUTHOR(S): Dejong, Gary (1); Telenius, Adele H.; Telenius, Hakan;

Perez, Carl F.; Drayer, Jan I.; Hadlaczky, Gyula

CORPORATE SOURCE: (1) Chromos Mol. Syst. Inc., 6660 Northwest Marine Drive,

Vancouver, BC V6T 1Z4 Canada

SOURCE: Cytometry, (Feb. 1, 1999) Vol. 35, No. 2, pp. 129-133.

ISSN: 0196-4763.

DOCUMENT TYPE: Article LANGUAGE: English

Background: A pilot production facility has been established to isolate AB mammalian artificial chromosomes at high purity by using flow cytometric techniques. Dicentric chromosomes have been generated by the targeted amplification of pericentric heterochromatic and centromeric DNA by activating the "megareplicator." Breakage of these dicentric chromosomes generates satellite DNA-based artificial chromosomes (SATAC) from 60 to 400 megabases. Methods: For large-scale production, we have developed cell lines capable of carrying one or two SATACs. A SATAC, because of a high adenine-thymine (Al) composition, is easily identified and sorted by using chromomycin A3 and Hoechst 33258 stains and a dual laser high-speed flow cytometer. A prototype SATAC (60 megabases) has been characterized. The prototype **SATAC** has been isolated from an original rodent/human hybrid cell line and transferred by using modified microcell fusion into a CHO production cell line. Results: Metaphase chromosomes from this production cell line were isolated in a modified polyamine buffer, stained, and sorted by using a modified sheath buffer that maintains condensed chromosomes. SATACs are routinely sorted at rates greater than 1 million per hour. Sorted SATACs have been transferred to a variety of cells by using microcell fusion technology and were found to be functional. Conclusions: By developing new SATAC containing cell lines with fewer numbers of chromosomes in conjunction with operating a high speed flow sorter we have effectively generated an efficient production facility geared purely for the isolation of SATACs.

3 ANSWER 10 OF 11 MEDLINE DUPLICATE 9

ACCESSION NUMBER: 83180419 MEDLINE

DOCUMENT NUMBER: 83180419 PubMed ID: 6301685

TITLE: Amplification of rDNA and type I sequences in Drosophila

males deficient in rDNA.

AUTHOR: de Cicco D V; Glover D M

SOURCE: CELL, (1983 Apr) 32 (4) 1217-25.

Journal code: 0413066. ISSN: 0092-8674.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198306

ENTRY DATE: Entered STN: 19900318

Last Updated on STN: 19990129 Entered Medline: 19830617

rDNA magnification is a heritable change in rDNA content that occurs in D. ABmelanogaster males when chromosomes deficient in rDNA are placed together for several generations. We have examined the restriction endonuclease cleavage pattern of the rDNA from an X chromosome undergoing magnification, and find no evidence for the selective amplification of either uninterrupted rDNA units or those containing insertion sequences. In addition, we observe an amplification of rDNA in the first generation of extremely bobbed male progeny to a level exceeding that of wild-type flies, but that reduces to the wild-type level in subsequent generations. The type I rDNA insertion elements also occur as tandem arrays, independently of rDNA. Southern hybridizations indicate that the majority of these sequences are located in the heterochromatin surrounding the nucleolus organizer on the X chromosome, and we find that they, too, amplify transiently in the first generation of magnifying males.

L48 ANSWER 1 OF 2 MEDLINE

ACCESSION NUMBER: 2001038301 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10954419 20411244

Novel generation of human satellite DNA-based artificial TITLE:

chromosomes in mammalian cells.

Csonka E; Cserpan I; Fodor K; Hollo G; Katona R; Kereso J; AUTHOR:

Praznovszky T; Szakal B; Telenius A; deJong G; Udvardy A;

Hadlaczky G

Institute of Genetics, Biological Research Center, CORPORATE SOURCE:

Hungarian Academy of Sciences, H-6701 Szeged, PO Box 521,

Hungary.

JOURNAL OF CELL SCIENCE, (2000 Sep) 113 (Pt 18) 3207-16. SOURCE:

Journal code: 0052457. ISSN: 0021-9533.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

200011

ENTRY DATE:

Entered STN: 20010322

Last Updated on STN: 20010322 Entered Medline: 20001129

An in vivo approach has been developed for generation of artificial ABchromosomes, based on the induction of intrinsic, large-scale amplification mechanisms of mammalian cells. Here, we describe the successful generation of prototype human satellite DNA-based artificial chromosomes via amplification-dependent de novo chromosome formations induced by integration of exogenous DNA sequences into the centromeric/ rDNA regions of human acrocentric chromosomes. Subclones with mitotically stable de novo chromosomes were established, which allowed the initial characterization and purification of these artificial chromosomes. Because of the low complexity of their DNA content, they may serve as a useful tool to study the structure and function of higher eukaryotic chromosomes. Human satellite DNA-based artificial chromosomes containing amplified satellite DNA, rDNA, and exogenous DNA sequences were heterochromatic, however, they provided a suitable chromosomal environment for the expression of the integrated exogenous genetic material. We demonstrate that induced de novo chromosome formation is a reproducible and effective methodology in generating artificial chromosomes from predictable sequences of different mammalian species. Satellite DNA-based artificial chromosomes formed by induced large-scale amplifications on the short arm of human acrocentric chromosomes may become safe or low risk vectors in gene therapy.

L48 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1997:718036 CAPLUS

DOCUMENT NUMBER: TITLE:

methods for prepg. mammalian artificial chromosomes

(MACs)

128:19355

INVENTOR(S):

Hadlaczky, Gyula; Szalay, Aladar A.

PATENT ASSIGNEE(S):

Hadlaczky, Gyula, Hung.; Szalay, Aladar A.; American Gene Therapy, Inc.; Biological Research Center of the Hungarian Academy of Sciences; Loma Linda University

SOURCE: PCT Int. Appl., 248 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| WO 9740183 | A2 | 19971030 | WO 1007 HCF011 | |
| WO 9740183 | A3 | 19980205 | WO 1997-US5911 | 19970410 |

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             LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ,
             VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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     EP 929689
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                                           EP 1997-920284
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     JP 2000508177
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                                                            19970410
PRIORITY APPLN. INFO.:
                                        US 1996-629822
                                                         A 19960410
                                        US 1996-682080
                                                         A 19960715
                                        US 1996-695191
                                                         A 19960807
                                        US 1996-682191
                                                         A 19960715
                                        WO 1997-US5911
                                                         W 19970410
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AB Methods for prepg. cell lines that contain artificial chromosomes, methods for prepn. of artificial chromosomes, methods for purifn. of artificial chromosomes, methods for targeted insertion of heterologous DNA into artificial chromosomes, and methods for delivery of the chromosomes to selected cells and tissues are provided. Also provided are cell lines for use in the methods, and cell lines and chromosomes produced by the methods. In particular, satellite artificial chromosomes [SATACs] that, except for inserted heterologous DNA, are substantially composed of heterochromatin, are provided. Methods for use of the artificial chromosomes, including for gene therapy, prodn. of gene products and prodn. of transgenic plants and animals are also provided.

=>

L46 ANSWER 13 OF 15 USPATFULL DUPLICATE 13

ACCESSION NUMBER:

94:15649 USPATFULL

TITLE: INVENTOR(S):

Mammalian artificial chromosomes Hadlaczky, Gyula, Szamos, Hungary

PATENT ASSIGNEE(S):

Biologic Research Center of the Hungarian Academy of

Sciences, Hungary (non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION:

US 5288625 19940222

APPLICATION INFO.:

US 1991-759558

19910913 (7)

DOCUMENT TYPE:

Utility

FILE SEGMENT:

Granted

PRIMARY EXAMINER:
ASSISTANT EXAMINER:

Schwartz, Richard A.

LEGAL REPRESENTATIVE:

Ketter, James

NUMBER OF CLAIMS:

Banner, Birch, McKie & Beckett

EYEMDIADY CLAIMS:

12

EXEMPLARY CLAIM: NUMBER OF DRAWINGS:

1 17 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT:

499

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB

4.1.

Non-human cell lines are disclosed which contain functional centromeres comprising human DNA sequences linked to a dominant marker gene. The centromeres are carried on stable chromosomes which carry no centromeres other than those comprising human DNA sequences. The cell lines can be used to isolate the chromosomes as well as for use in inserting genes into mammalian cells. Methods are taught for generating such cell lines from cell lines carrying dicentric chromosomes.

L46 ANSWER 11 OF 15 MEDLINE DUPLICATE 11

ACCESSION NUMBER: 96385350 MEDLINE

DOCUMENT NUMBER: 96385350 PubMed ID: 8793208

TITLE: De novo chromosome formations by large-scale amplification

of the centromeric region of mouse chromosomes.

AUTHOR: Kereso J; Praznovszky T; Cserpan I; Fodor K; Katona R;

Csonka E; Fatyol K; Hollo G; Szeles A; Ross A R; Sumner A

T; Szalay A A; Hadlaczky G

CORPORATE SOURCE: Institute of Genetics, Hungarian Academy of Sciences,

Szeged, Hungary.

SOURCE: CHROMOSOME RESEARCH, (1996 Apr) 4 (3) 226-39.

Journal code: 9313452. ISSN: 0967-3849.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199612

ENTRY DATE: Entered STN: 19970128

Last Updated on STN: 19970128 Entered Medline: 19961209

Chromosomes formed de novo which originated from the centromeric region of ABmouse chromosome 7, have been analysed. These new chromosomes were formed by apparently similar large-scale amplification processes, and are organized into amplicons of approximately 30 Mb. Centromeric satellite DNA was found to be the constant component of all amplicons. Satellite DNA sequences either bordered the large euchromatic amplicons (E-type amplification), or made up the bulk of the constitutive heterochromatic amplicons (H-type amplification). Detailed analysis of a heterochromatic megachromosome formed de novo by an H-type amplification revealed that it is composed of a tandem array of 10-12 large (approximately 30 Mb) amplicons each marked with integrated "foreign' DNA sequences at both ends. Each amplicon is a giant palindrome, consisting of two inverted doublets of approximately 7.5-Mb blocks of satellite DNA. Our results indicate that the building units of the pericentric heterochromatin of mouse chromosomes are approximately 7.5-Mb blocks of satellite DNA flanked by non-satellite sequences. We suggest that the formation de novo of various chromosome segments and chromosomes seen in different cell lines may be the result of large-scale E- and H-type amplification initiated in the pericentric region of chromosomes.

L46 ANSWER 10 OF 15 MEDLINE DUPLICATE 10

ACCESSION NUMBER: 96385351 MEDLINE

DOCUMENT NUMBER: 96385351 PubMed ID: 8793209

TITLE: Evidence for a megareplicon covering megabases of

centromeric chromosome segments.

1

AUTHOR: Hollo G; Kereso J; Praznovszky T; Cserpan I; Fodor K;

Katona R; Csonka E; Fatyol K; Szeles A; Szalay A A;

Hadlaczky G

CORPORATE SOURCE: Institute of Genetics, Hungarian Academy of Sciences,

Szeged, Hungary.

SOURCE: CHROMOSOME RESEARCH, (1996 Apr) 4 (3) 240-7.

Journal code: 9313452. ISSN: 0967-3849.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199612

ENTRY DATE: Entered STN: 19970128

Last Updated on STN: 19970128 Entered Medline: 19961209

We have analysed the replication of the heterochromatic megachromosome AB that was formed de novo by a large-scale amplification process initiated in the centromeric region of mouse chromosome 7. The megachromosome is organized into amplicons approximately 30 Mb in size, and each amplicon consists of two large inverted repeats delimited by a primary replication initiation site. Our results suggest that these segments represent a higher order replication unit (megareplicon) of the centromeric region of mouse chromosomes. Analysis of the replication of the megareplicons indicates that the pericentric heterochromatin and the centromere of mouse chromosomes begin to replicate early, and that their replication continues through approximately three-quarters of the S-phase. We suggest that a replication-directed mechanism may account for the initiation of large-scale amplification in the centromeric regions of mouse chromosomes, and may also explain the formation of new, stable chromosome segments and chromosomes.